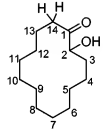
REMARKS

The claims pending in the present Application are claims 1-19, 21-37, 48-64 and 71-78. Applicant amends variables R^3, R^4, and R^6 throughout to revise the scope of genus presented by Applicant. Applicant also takes the opportunity to correct typographical and syntax errors throughout. No new matter has been added by these amendments.

I. **Rejection under 35 U.S.C. §102(b)**

Claims 1-2 and 49 are rejected under 35 U.S.C. §102(b) as being anticipated by Singh et al. [Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (2002), 41B(2), 423-426]. Specifically, the compound of Singh et al. has the following structure:



2-hydroxycyclotetradecanone,

and corresponds to Applicant's claimed compound wherein n is 3; each of R_a, R_b, R_1, R_2, R_3, Y_1, Y_2, and Q are defined as hydrogen; X_1 is defined as $CR^{X1}R^{X2}$, wherein R^{X1} and R^{X2} are defined as hydrogen; and R_4 is defined as "oxo". Applicant has amended claims 1, 2 and 49 to eliminate the possibility that R_6 = hydrogen, i.e., R_6 now requires something other than hydrogen. Applicant respectfully submits that the above amendment renders the rejection under 35 U.S.C. §102(b) moot.

II. **Rejection under 35 U.S.C. §112, para. 1**

Claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73 and 76-78 stand rejected under 35 U.S.C. §112, first paragraph. The Examiner alleges that the specification, while being enabling for the

compounds identified as having the asserted utility with experimental data, does not reasonably provide enablement for the asserted utility of the entirety of the claim scope. Applicant is surprised and disappointed by this rejection under 35 USC 112, first paragraph.

As an initial matter, Applicant respectfully submits that the Examiner has overlooked significant enablement provided by the specification demonstrating effective biological activity of claimed compounds, and compositions containing them. The Examiner asserts (at page 5 of the Office Action) that Applicant provides data for what appears to be only 4 compounds when considering the "Number of Working Examples and Guidance Provided by Applicant." The Examiner is incorrect.

The present specification includes a variety of biological data including, for example, (1) tube formation assay data (3 compounds; see for example Table 1, paragraph [0364]); (2) wound healing assay data (2 compounds; see for example Table 2, paragraph [0365]); (3) chamber cell migration assay data (16 compounds; see for example Tables 4-6, paragraphs [0432]-[0438]) . Applicant reminds the Examiner that the present invention was not made in a vaccum. It was made in the context of significant information about *migrastatin*, which is a natural compound, *known in the art* prior to the filing of the present application. Migrastatin was known to be useful, among other things, to inhibit both migration and anchorage-independent growth of human tumor cells (see page 1, paragraph [0004]).

In the context of what was known about migrastatin and its biological activities, the present specification provides more than sufficient guidance to demonstrate the activity and utility of the claimed compounds. The Examiner provides no reason to doubt the assertions made in the specification regarding the activity and utility of the claimed compounds and compositions. Applicant emphasizes that case law holds that "in order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)...A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is *a reason to doubt*

the objective truth of the statements contained therein which must be relied on for enabling support." (see MPEP 2164.04, emphasis added). In light of the provided data establishing activity of claimed compounds, together with the understanding in the art of migrastatin's activities and the reasonable assertions in the specification, it is clear that all requirements of 35 USC 112 are met and the rejection should be removed.

Furthermore, Applicant respectfully points out that many of the claims (e.g., claims 1-48) in the present case are directed to *compounds* rather than to *pharmaceutical compositions*, or to *methods of treating* any particular disease, disorders or conditions. Given that the claimed compounds are related in structure to migrastatin, they are useful, among other things, as intermediates in the preparation of migrastatin, as reagents for characterizing migrastatin, and/or as inhibitors of cell migration. In addition, the present specification demonstrates that claimed compounds exhibit antiangiogenic activity, and/or have an anti-proliferative effect (see page 2, paragraph [0007] of the present specificaation). The specification specifically addresses some or all of these uses, each and every one of which would be immediately apparent to those of ordinary skill in the art upon reading the application as filed. Thus, the present specification fully enables claims to the compounds themselves (e.g., claims 1-48) *both* based on their utility in the preparation, characterization, and/or use of migrastatin, and *also* based on their independent utility related to their biological activities, shared with migrastatin.

The Examiner has apparently failed to appreciate the various utilities of claimed compounds relating to the preparation, characterization and/or use of migrastatin, and has levied the lack of enablement rejection *solely* on the ground that Applicant has not fully demonstrated the biological activity of every claimed compound, and the mechanism of that activity. Specifically, the Examiner describes the "issue" with respect to enablement as:

> "whether the specification provides embodiments allowing use of the claimed invention without requiring undue experimentation by one of ordinary skill in view of the highly unpredictable nature of inhibiting enzymes or unknown pathways" (page 4 of the Office Action, third paragraph).

Thus, the Examiner has *completely ignored* many apparent utilities of presently claimed compounds and has rejected the claims based on a speculation that not all of them would

effectively inhibit the same biological enzyme(s). For this reason alone, the rejection should be removed with respect to claims 1-48.

Still further, Applicant is puzzled by the current rejection for lack of enablement of current claims 49-55, directed to pharmaceutical compositions, given that pharmaceutical composition claims of *almost identical scope* had previously been found *by the same examiner* to satisfy the requirements of 35 USC 112. The present case is a 35 U.S.C. §371 national stage entry filing of PCT/US04/09571 (the '571 application), and is a "sister" case to a 35 U.S.C. §371 national stage entry filing of PCT/US04/009380 (the '380 application), which claims priority to the same two provisional applications as does the '571 application. The *text* of the '380 specification is almost identical to that of the present application; the '380 specification does not add any additional support relevant to such composition claims.

In the '380 application, claims to pharmaceutical compositions and methods were initially presented with respect to a genus of compounds significantly broader than that examined in the present case. The *present* Examiner, who is handling prosecution of both the '380 application and the present case, rejected those broad claims (specifically, claims 1-40 and 43-62) in the '380 application under 35 U.S.C. §112. No lack of enablement rejection was levied against pharmaceutical composition claims.

In the '380 application, Applicant fully addressed the Examiner's rejections in a Response dated December 5, 2008, which Response included an amendment to the claims substantially reducing their scope to largely match the compound claim scope examined in the present case. Appropriately, that Response overcame the 112 rejection with respect to the pharmaceutical compositions[1], and the same was acknowledged in the next Office Action, dated 2/13/09. Thus, as of at least 2/13/09, the Examiner had acknowledged that claims to pharmaceutical compositions of a scope very similar to that of presently pending pharmaceutical composition claims (claims 49-55) met all requirements of 35 USC 112.

Further Office Actions were issued in the '380 application on April 17, 2009 (Advisory Action) and July 21, 2009 (Non-Final Office Action). Neither of these actions contained any

[1] The lack of written description rejection was also removed with respect to the method claims, but the lack of enablement rejection was maintained until those method claims were subsequently canceled.

rejections under 35 USC 112, first paragraph. The claims examined in the present case were first submitted on 7/8/2009, and were specifically crafted to closely mimic the compound scope found in the '380 application's pharmaceutical composition claims, since the above-referenced prosecution in the '380 application had confirmed that such scope satisfied 35 USC 112.

The MPEP §706 recites the following:

> The goal of examination is to clearly **articulate any rejection early in the prosecution process** so that the applicant has the opportunity to provide evidence of patentability and otherwise reply completely at the **earliest opportunity**. The examiner then reviews all the evidence, including arguments and evidence responsive to any rejection, before issuing the next Office action. Where the examiner determines that information reasonably necessary for the examination should be required from the applicant under 37 CFR 1.105, such a requirement should generally be made either prior to or with the first Office action on the merits and should follow the procedures in MPEP § 704.10 *et seq*. (Emphasis added by Applicant).

The first Office Action was issued in the '380 application on 11/26/07. Between that time and February 201 (i.e., over *more than 2 years of examination, including 4 Office Actions, 1 Advisory Action, and 2 interviews*), the Examiner *never* levied a rejection for lack of enablement of the pharmaceutical composition claims in that case, and levied only a single rejection for lack of written description, which rejection was overcome by amendment to a compound scope very similar to that pending in the present case. That the Examiner is *now* levying a lack of enablement rejection of such claims (levied in the '380 application in a new Office Action issued on 2/1/2010, and levied in the present case in the Office Action of 10/14/2009), is a clear violation of MPEP §706. Delayed examination of this sort deprives Applicant of proper patent protection; should the rejection be maintained, Applicant respectfully requests an award of full patent term adjustment for the entirety of the PTO's delay in levying the rejection (from at least 11/26/2007 to at least 10/14/2009).

For at least all of these reasons, Applicant respectfully submits that the rejection for lack of enablement in the present case should be removed.

III. **Provisional Double Patenting Rejection**

Claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73 and 76-78 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-42 and 45-47 of copending application serial number 10/551,152.

Applicant respectfully submits, and the Examiner correctly states, that the rejection of claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73 and 76-78 under the judicially created doctrine of obviousness-type double patenting is premature because no claim of application serial number 10/551,152 has been patented. In view of the provisional nature of this rejection, Applicant holds this rejection in abeyance to be addressed when a relevant claim of US application serial number 10/551,152 issues. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1-5, 7-13, 23-24, 34-35, 49-55, 71-73 and 76-78 and acknowledge patentability of the same.

Applicant invites the Examiner to contact the undersigned, Julie Anne Knight, at (617) 248-5227, with any questions pertaining to the above-identified application in order to expedite prosecution of this case.

Respectfully submitted,

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